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RÉSUMÉ

L'auteur résume son expérience avec l'emploi du flaxédyl chez cent opérés par comparaison à cent autres où le curare fut employé. Ce nouvel agent curarisant de synthèse est une addition de valeur aux médicaments employés couramment par l'anesthésiste. Comme avec le curare le patient peut subir n'importe laquelle intervention chirurgicale tout en ne recevant que de très petite doses d'agents anesthésiques. Il est supérieur au curare parce qu'il ne produit pas ni de spasme bronchique ni d'hypotension. De plus la respiration est déprimée à un moindre degré. Cependant l'auteur a souvent remarqué qu'une tachycardie d'ailleurs bénigne se produisait. Les contre-indications sont les mêmes qu'avec le curare. Il n'est pas nécessaire d'employer d'aussi grosse dose qu'avec le curare lorsque le cyclo est l'agent anesthésique. YVES PRÉVOST

CONVULSIONS AND HEMIPLEGIA IN PERTUSSIS PROPHYLAXIS

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MILD to moderately severe local and febrile reactions to pertussis vaccine are commonly encountered, and have not caused great concern. Recent studies in the United States have, however, indicated that grave reactions may occur on rare occasions following the use of pertussis vaccine and other biological products. These include convulsive seizures with or without permanent cerebral damage. A number of these have ended fatally. Such reactions have not been reported in Canada to date, despite the widespread use of pertussis vaccine over the past decade.

As early as 1933 Madsen[1] reported that two infants in Denmark in the neonatal period had died shortly after the administration of pertussis vaccine. In 1948 Byers and Moll[2] reported in detail on encephalopathy following the use of this vaccine. During the period between 1939 and 1947 there had been fifteen instances in which admissions had been made to the Children's Hospital of Boston for this complication; two of these cases died. In the same period there were 8 admissions for cerebral damage following smallpox vaccination, and 26 cases in which encephalopathies occurred following pertussis infection. They also reviewed the literature on these complications in pertussis prophylaxis.

In 1949 Toomey[3] reported on information received after solicitation from a large number of physicians who were concerned with pertussis immunization. The replies indicated 38 instances in which reactions occurred that were sufficiently severe to produce convulsions. Two of these cases are known to have died.

Following are descriptions of two cases in which severe untoward reactions occurred after administration of the triple antigen preparation* most commonly used in this country at the present time.

CASE 1

C.H., a white female infant of seven months received the first dose of multiple antigen in my office on May 28, 1948. Five hours later the mother noticed a general reaction consisting of fever with malaise and irritability. Nine hours after inoculation the mother reported the occurrence of a convulsion, and the baby was seen in the early stage of seizure. The clonic movements were predominantly right-sided, involving the right arm, right leg, and right side of the face; the head was kept turned to the right. In spite of the evident deep coma, shrill shrieking noises were emitted during the most violent phase of the seizure, which lasted well over two hours. The highest rectal temperature recorded during the convulsive seizure and afterwards was 102°. Phenobarbital sodium and rectal chloral hydrate were used to control the spasms.

Twitchings of the right side of the body recurred for the next two days in milder form. On admission to the London War Memorial Children's Hospital, on May 31, Dr. H. S. Little was consulted. There was little active use of the right arm and leg and there was paresis of the right sixth and seventh cranial nerves. Mild twitchings of the right side of the body continued, and spasticity was noted in the right arm and leg. The eyegrounds appeared normal. It was felt at this time that some permanent cerebral damage had occurred involving principally the left cerebral hemisphere. On June 2 the patient was transferred to the Toronto Hospital for Sick Children for further investigation. On discharge from that hospital two days later there was slight noticeable improvement in voluntary movement of the affected arm and leg; the twitchings had ceased.

Spinal fluid was under normal pressure; 2 cells per c.mm.; 25 mgm. total protein, 60 mgm. sugar, 745 mgm. chlorides %. Colloidal gold reaction was negative. Hb. 12.6 gm. %, white blood cells 8,200. Blood Wassermann was negative. Serum Ca. 11.1 and P. 4.8 mgm. %. Fasting blood sugar 110 mgm. %.

Further progress.—On June 30, neurological examination was made by Dr. W. S. Keith in Toronto. He reported that there was fairly good return of function of the sixth and seventh cranial nerves, but due to persistence of hemiparesis of right arm and leg, he felt that there had been considerable and fairly persistent damage to the left parietal and frontal lobes.

On September 12, the patient was again admitted to the War Memorial Children's Hospital in a convulsive seizure accompanying an attack of acute otitis media. On this occasion the rectal temperature rose to 104° F. The convulsion was rapidly controlled and recovery was prompt when the acute infection subsided. There was no evidence of further residual encephalopathy following this episode.

Improvement of function of the right leg has been greater than that of the right arm. She was able to walk unaided at fifteen months of age. At first the gait was of the typical hemiplegic type with the right

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leg swinging out a good deal; this has noticeably improved. Some atrophy is still present in the muscles of the right leg but atrophy is more marked in the right arm, especially in the forearm and hand. Mild seizures of petit mal type have occurred at frequent intervals during the past year but these have become rare in the past few months. At twenty-nine months of age speech is much retarded. In the field of behaviour there is marked restlessness both day and night, destructiveness, and inability to concentrate on normal play; this has necessitated psychiatric guidance.

Past history.—This patient was born full term and delivery was normal. Birth weight was 6 lb. 10 oz. At seven months the weight was 17 lb. Development was normal up until the time of administration of triple antigen when the infant was seven months of age. A paternal aunt and uncle died in infancy in convulsions of undetermined origin.

The preparation used was a fluid form of diphtheria toxoid, pertussis vaccine and tetanus toxoid (combined). The dose given was ½ c.c. which contained approximately 11¼ billion killed bacilli from strains in Phase I. H. pertussis, 15 Lf's of diphtheria toxoid and 5 Lf's of tetanus toxoid. It has been my practice for several years to use this smaller initial dose in an effort to minimize the general reactions commonly encountered.

CASE 2

V.R., a white 3-year old girl received the third dose of triple antigen on December 13, 1949, through the City Department of Health immunization program. Eleven hours later vomiting occurred and a convulsive seisure followed shortly; she was admitted to the War Memorial Children's Hospital. Loud shrill noises were present during the stage of clonic movements. The twitching was most marked on the left side of the body including the face. Rectal temperature did not exceed 100.2° F. Symptoms were controlled within an hour by the use of phenobarbital sodium. She was discharged from hospital in two days without evidence of permanent cerebral damage.

Past history.—She was born two months prematurely, weighing 3 lb. 4 oz.; development was normal; she talked at twelve months. There was a previous admission to War Memorial Children's Hospital on October 23, 1949, in a generalized convulsive seizure. An acute tonsillitis was present; the rectal temperature was 102° F. She had received her first dose of triple antigen thirty-eight hours previously. Recovery was rapid and complete when the infection cleared. The second dose of triple antigen resulted only in some malaise during the same evening. The family history disclosed that a paternal aunt and uncle had suffered from convulsions.

The preparation used in this case was similar to that of Case 1. The amount injected at each inoculation was 1 c.c. which contained approximately 22½ billion killed bacilli from strains in Phase I. H. pertussis, 30 Lf's of diphtheria toxoid and 10 Lf's of tetanus toxoid.

COMMENT

The convulsions which occurred in these two cases differed from the usual febrile convulsions in some respects. The fever attained was lower than that usually associated with the febrile convulsive state. The convulsive movements were predominantly one-sided; right-sided in Case 1, and left-sided in Case 2. During the period of coma there was prolonged stimulation of the voice mechanism causing shrill shrieking noises.

Both cases showed other evidence of convulsive tendency. In Case 1 a convulsive seizure occurred three months after the initial one when a middle ear infection developed. In Case 2 a preceding convulsion had occurred during an attack of acute tonsillitis; whether the first inoculation given thirty-eight hours previously contributed to the attack is problematical. In both cases there was some family history of convulsions.

In Case 1 the clinical manifestations of the encephalopathy produced were similar in many respects to those which may occur following pertussis infection. Litvak *et al.*[4] have recently reviewed the latter type of encephalopathy in detail.

The mechanism which may produce a dangerous reaction is not clear, although a variety of possibilities has been suggested. The only common factor in all cases reported was the use of some form of pertussis antigen. In two of the reports previously mentioned[2, 3] the products of at least eight manufacturers had been employed in the immunizing procedures. In most cases fluid pertussis vaccines were used; a few preparations were combinations with diphtheria toxoid and tetanus toxoid; in one triple antigen the pertussis component was alum-precipitated. A fatal case of Globus and Kohn[5] had received a detoxified formolized filtrate of pertussis antigen vaccine.

No specific therapy has been suggested for the treatment of these untoward reactions. It is doubtful if any of our available agents could have material effect in modifying the amount of cerebral damage once a severe reaction occurs. There is not sufficient evidence to indicate that the incidence of grave results with pertussis vaccine outweighs the obvious advantages of immunization. However, the evidence thus far indicates that there is an increased danger of permanent encephalopathy in those subjects who have previously demonstrated a tendency toward the convulsive state, in whom there is a family history of convulsions or in those who already have some disease of the central nervous system. Under these conditions, if used at all, the antigen should be administered in decreased dosage. It seems superfluous to add that it

should be withheld in cases of infection, especially those accompanied by fever.

SUMMARY

Two cases have been described in which severe untoward reactions followed administration of multiple antigens for prophylactic immunization. The pertussis component of the preparation is considered responsible for the adverse effects produced.

In Case 1 an explosive episode occurred with severe prolonged convulsive seizure and right-sided hemiplegia. Sequelæ remain which are indicative of permanent cerebral damage. In Case 2 the reaction was less violent; recovery following the convulsive seizure has been complete.

Some differences have been noted in the clinical character of the convulsive seizures in these cases as compared with the more frequent febrile convulsions. It is suggested that the severe reactions resemble some of those encountered in pertussis infection.

Reference has been made to other reports of similar untoward effects occurring with pertussis preparations of various types alone or in different combinations with other antigens and manufactured by a number of companies.

Attention has been drawn to the serious results which may occur when pertussis antigen is administered to a subject who is predisposed to the convulsive state.

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FRIEDLANDER'S BACILLUS MENINGITIS*

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IN 1882 Friedländer announced the discovery of a micro-organism which he believed to be the cause of lobar pneumonia and which has since borne his name. It is now included under the genus Klebsiella, the members of which are encountered in diseases of the respiratory tract, but are not infrequently isolated from suppurative processes in various sites throughout the body and may even give rise to a septicæmia. Weichselbaum[1] in 1888 reported the first case of meningitis due to the *B. Friedländeri*. That the condition is rare is indicated by the various statistical studies available. In 1931 Rothschild[2] found only one case in the American literature and this one ended fatally.[3] His own case recovered following adequate surgical drainage of a subdural abscess secondary to otitis media and mastoiditis, and is the only incontestable case with recovery prior to sulfonamide therapy. MacKay[4] (quoting Neal's statistics) found 6 instances of *B. Friedländeri* meningitis in 3,599 cases of meningitis. Jacob and Top[6] reported 7 in a total of 3,377 cases of meningitis in their study. Ransmeier and Major[7] in a careful review of the literature up to 1943 found only 29 cases and added one of their own to the list. Since that time 24 additional cases have been reported, according to Sadusk *et al.*,[8] in 1948. This number can be now increased in view of reports by Jacob and Top,[6] and Jobin and Lessard.[9] No doubt there have been other cases either unrecognized or unreported.

The rarity of Friedländer's bacillus meningitis and the comparatively small number of successfully treated cases to date, prompted the present report of one which had a favourable outcome.

CASE REPORT

Mr. J.F., aged 57, was admitted to the medical service of the Victoria General Hospital on December 14, 1948, in a semi-comatose state. The patient had been in the surgical service from September 6 to September 30, with a severe attack of what was considered to be obstructive jaundice. His family and personal history were non-contributory except for a back injury in 1917.

On this second admission, a brief history obtained from his brother indicated that the patient had been apparently quite well since leaving hospital until the evening of December 11, when he had a chill and next morning he was confused and vomiting, but had no headache, earache, or pain of any kind. The temperature was 95.4; pulse rate 116; respiratory rate 32. Physical examination was rendered difficult by the patient's extreme restlessness and irritability. He was very thin. The face was florid and the skin was dry and lax, but no icterus was evident. Respirations were noisy and rapid. The mouth was kept tightly closed and the breath was offensive. There was definite rigidity of the neck. The eyes were open and fixed, with pupils contracted, equal and responsive to light. Fundi were normal. There was an old perforation of the left ear drum but no evidence of active infection in either ear. The nose was clear. Examination of the heart, lungs and abdomen was negative. Blood pressure 120/84. The reflexes were diminished and Babinski's sign absent. Kernig's and Brudzinski's signs were positive. A tentative diagnosis of meningitis was made. The cerebrospinal fluid was turbid but not under pressure; sugar—none; colloidal curve—meningitic; abundant pus cells, too numerous to count accurately. Micro-organisms in the smear resembled pneumococci. The urine was negative except for a trace of albumin, Hb. 15.2 gm., red blood

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